Establishing a Female-only Controlled Human Schistosoma mansoni Infection Model: a safety and dose finding study (CoHSI2)

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Primary Objective: - To investigate the safety, tolerability and attack rate of female Schistosoma mansoni cercariae in healthy Schistosome-naïve volunteers Exploratory Objectives: - To investigate the kinetics of circulating anodic antigen (CAA)...

Ethical review	Approved WMO
Status	Completed
Health condition type	Helminthic disorders
Study type	Interventional

Summary

ID

NL-OMON54881

Source
ToetsingOnline

Brief title
CoHSI2

Condition

- Helminthic disorders

Synonym
bilharzia, Schistosomiasis

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: Infectious diseases, Schistosoma mansoni, Schistosomiasis, Tropical medicine

Outcome measures

Primary outcome

Main study parameter/endpoint:

• Frequency and severity of adverse events after controlled human Schistosoma mansoni infection with female cercariae.

• The number of female cercariae at which 100% volunteers show detectable Schistosoma mansoni circulating anodic antigen

Secondary outcome

Other study parameters/endpoints:

• Time to positive serum and urine CAA test

• Comparison of the peak serum CAA concentration in different dose groups

• Humoral (antibody) response directed against Sm antigens

• Cellular responses directed against Sm antigens

• Changes in microbiome after controlled human Schistosoma mansoni infection with female Sm cercariae

Study description

Background summary

Schistosomiasis is a parasitic disease of global importance, for which no vaccine exists. Vaccine candidates are tested for efficacy in large-scale Phase 2 and 3 field trials in Schistosoma-endemic areas, where the endpoint is usually the incidence of infection or disease following natural exposure. Such

trials therefore require long duration and/or large population sizes in order to obtain a good estimate of the effect size. Conducting controlled, experimental infection studies have been shown to eliminate several drawbacks of the traditional proof-of-efficacy approach. Previously, we have established a male-only controlled human Schistosoma mansoni infection model, that proved to be safe and well-tolerated in healthy Schistosoma-naïve healthy volunteers. In this study we aim to develop a female-only controlled human Schistosoma mansoni infection model that can be used to provide early proof-of-concept data on candidate schistosomiasis vaccines and serve as a platform to study schistosome immune responses. This is of particular relevance as one of the developed schistosomiasis vaccine candidate*s target antigens is preferentially expressed on female schistosomes.

Study objective

Primary Objective:
- To investigate the safety, tolerability and attack rate of female Schistosoma mansoni cercariae in healthy Schistosome-naïve volunteers
Exploratory Objectives:
- To investigate the kinetics of circulating anodic antigen (CAA) after infection with female Schistosoma mansoni cercariae in healthy Schistosome-naïve volunteers
- To investigate immunological, metabolic and microbiome changes after infection with Schistosoma mansoni female cercariae
- To explore potential differences in CAA kinetics and immunological responses after infection with male or female Schistosoma mansoni cercariae

Study design

Open label, dose escalation intervention study with adaptive design

Intervention

Groups of 3 or 7 volunteers will be exposed to a pre-defined number of female cercariae. Depending on the outcome of infection and safety data, the dose will be escalated or additional volunteers will be exposed to the same number of cercariae. Volunteers will visit the clinical trial centre weekly after infection to record adverse events.

Study burden and risks

Volunteers will be requested to visit the trial centre on a weekly basis for 16 weeks. After this bi-weekly visits will follow until week 20. Final follow up visit will be after one year. Blood and urine sampling will take place at every visit. Nasosorption sampling is performed during the first eight weeks. They will keep a diary to record adverse events during 20 weeks. Volunteers will be

dermally exposed to female cercariae once. They may experience adverse events, related to acute schistosomiasis syndrome with fatigue, malaise, and fever. At 8 weeks and 12 weeks after infection, they will be treated with praziquantel to cure the Schistosoma infection. Praziquantel is known to potentially give fatigue, gastrointestinal side effects, and dizziness. There is no benefit to participation in the trial.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Subject is aged >= 18 and <= 45 years and in good health.
2. Subject has adequate understanding of the procedures of the study and agrees to abide strictly thereby.
3. Subject is able to communicate well with the investigator, is available to

attend all study visits.
4. Subject will remain within Europe (excluding Corsica) during the study period and is reachable by mobile telephone from week 3 to week 8 of the study period.
5. Subject agrees to refrain from blood donation to Sanquin or for other purposes throughout the study period.
6. For female subjects: subject agrees to use adequate contraception and not to breastfeed for the duration of study.
7. Subject has signed informed consent.

Exclusion criteria

1. Any history, or evidence at screening, of clinically significant symptoms, physical signs or abnormal laboratory values suggestive of systemic conditions, such as cardiovascular, pulmonary, renal, hepatic, neurological, dermatological, endocrine, malignant, haematological, infectious, immune-deficient, psychiatric and other disorders, which could compromise the health of the volunteer during the study or interfere with the interpretation of the study results. These include, but are not limited to, any of the following:
- body weight <50 kg or Body Mass Index (BMI) <18.0 or >30.0 kg/m2 at screening;
- positive HIV, HBV or HCV screening tests;
- the use of immune modifying drugs within three months prior to study onset (inhaled and topical corticosteroids and oral anti-histamines exempted) or expected use of such during the study period;
- history of malignancy of any organ system (other than localized basal cell carcinoma of the skin), treated or untreated, within the past 5 years;
- any history of treatment for severe psychiatric disease by a psychiatrist in the past year;
- history of drug or alcohol abuse interfering with normal social function in the period of one year prior to study onset.
2. The chronic use of any drug known to interact with praziquantel, artesunate or lumefantrine metabolism (e.g. phenytoïn, carbamazepine, phenobarbital, primidon, dexamethason, rifampicine, cimetidine, flecaïnide, metoprolol, imipramine, amitriptyline, clomipramine, class IA and III anti-arrythmics, antipsychotics, antidepressants, macrolides, fluorchinolones, imidazole- and triazole antimycotics, antihistamines) Because lumefantrine may cause extension of QT-time, chronic use of drugs with effect on QT interval are excluded from the study.
3. For female subjects: positive urine pregnancy test at screening.
4. Any history of schistosomiasis or treatment for schistosomiasis.
5. Positive serology for schistosomiasis or elevated serum CAA at screening.
6. Known hypersensitivity to or contra-indications (including co-medication) for use of praziquantel, artesunate or lumefantrine.
7. Being an employee or student of the department of parasitology or infectious

diseases of the LUMC

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-08-2020
Enrollment:	22
Type:	Actual

Ethics review

Approved WMO Date:	17-05-2020
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	01-03-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04269915
CCMO	NL72661.058.20

Study results

Date completed: 12-12-2022

Results posted: 12-10-2023

Summary results
Trial ended prematurely

First publication
12-10-2023